

SITC 2019

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& Convention Center

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NATIONAL HARBOR, MARYLAND



Society for Immunotherapy of Cancer



CD122-selective IL-2 complexes treat ovarian carcinoma by inhibiting regulatory T cells and promoting T cell stem cells

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Society for Immunotherapy of Cancer

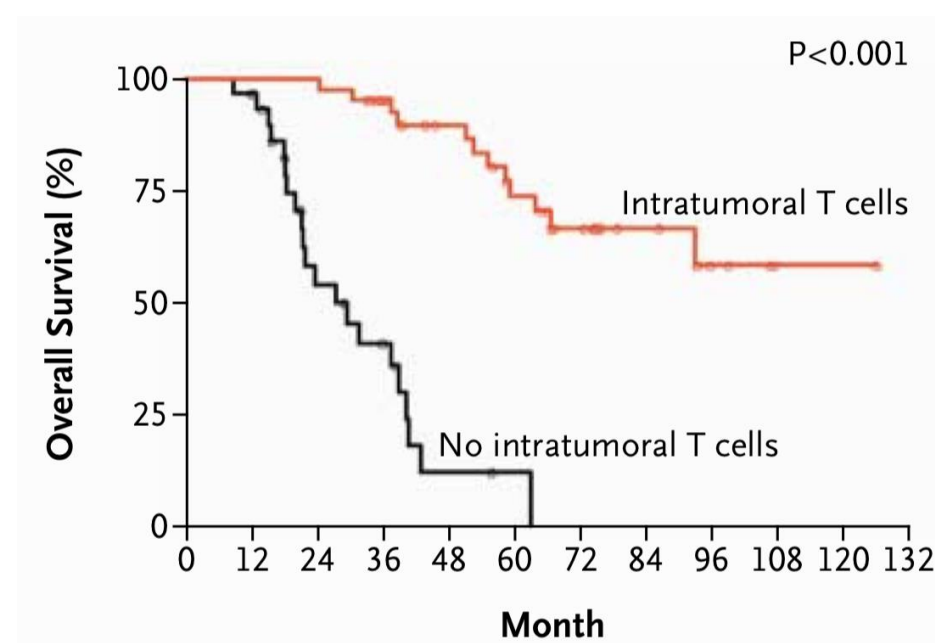
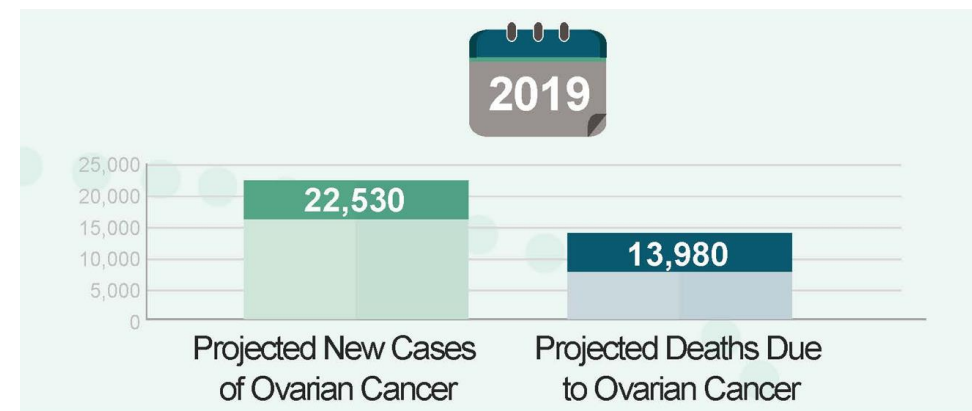
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Disclosure

- Authors have nothing to disclose

Ovarian Cancer (OC)

- Leading cause of gynecological cancer-related death in western countries
- More than 80% of patients die of recurrent disease after first-line therapy
- Intratumoral T cells presence positively correlates with survival of OC patients
- Poorly respond to immune checkpoint blockade (ICB) therapy



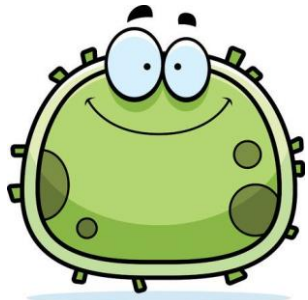
gemstoneoncology.com

Zhang et al, N Engl J Med 2003;348:203-13.

IL-2 and IL-2 receptor

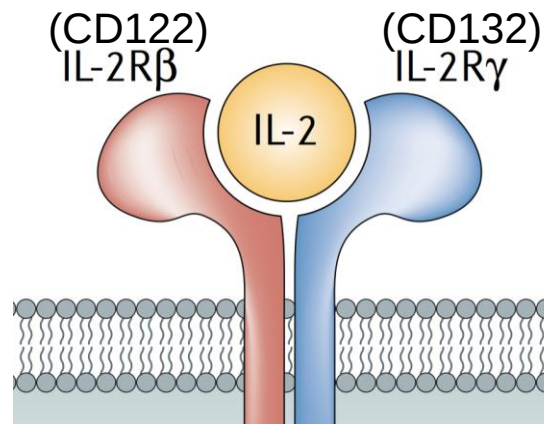
- Approved in 1992 for metastatic renal cell carcinoma; in 1998 for metastatic melanoma
- Toxic and ineffective

**CD8+ Effector T cells
(Teffs)**

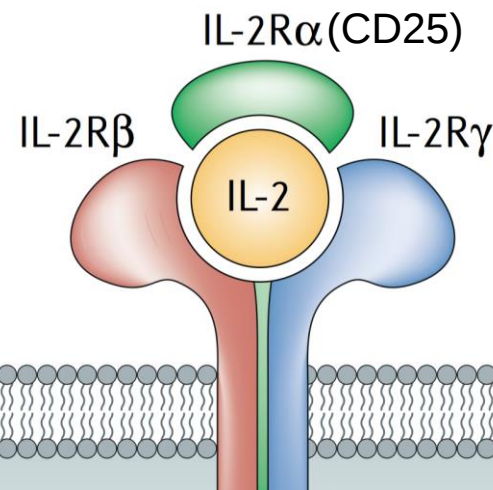


Tumor Killing

Intermediate affinity



High affinity



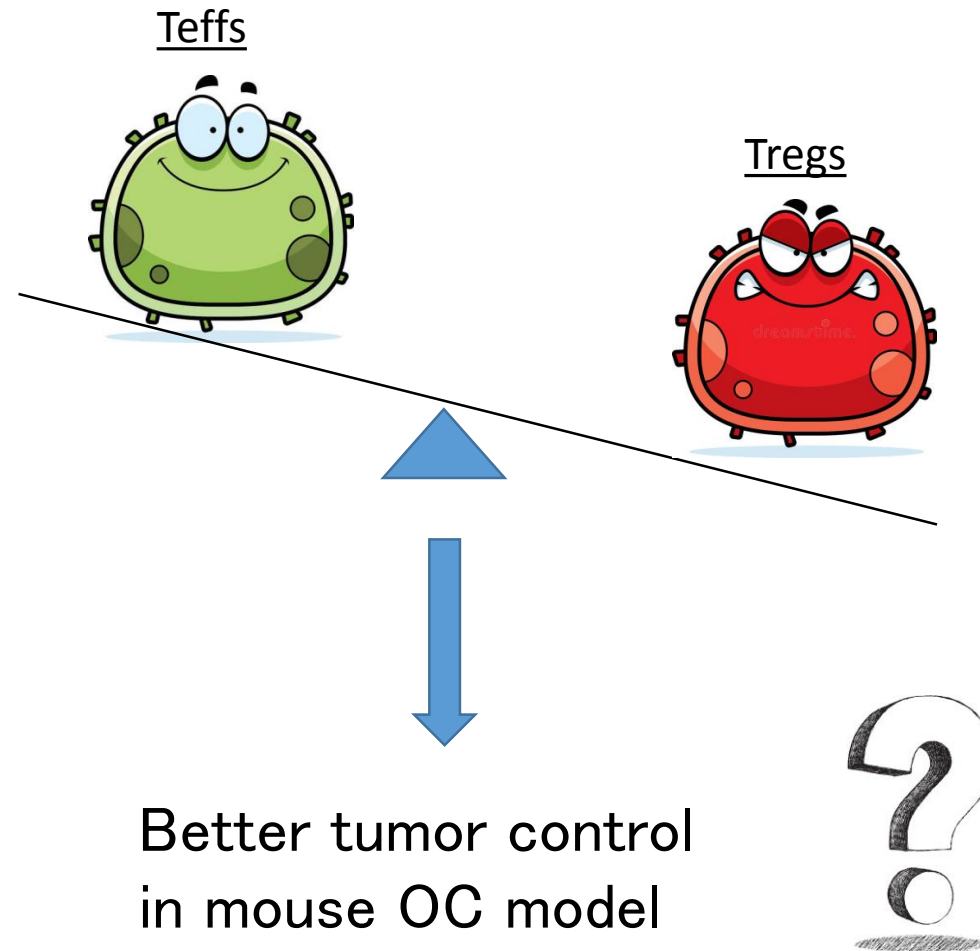
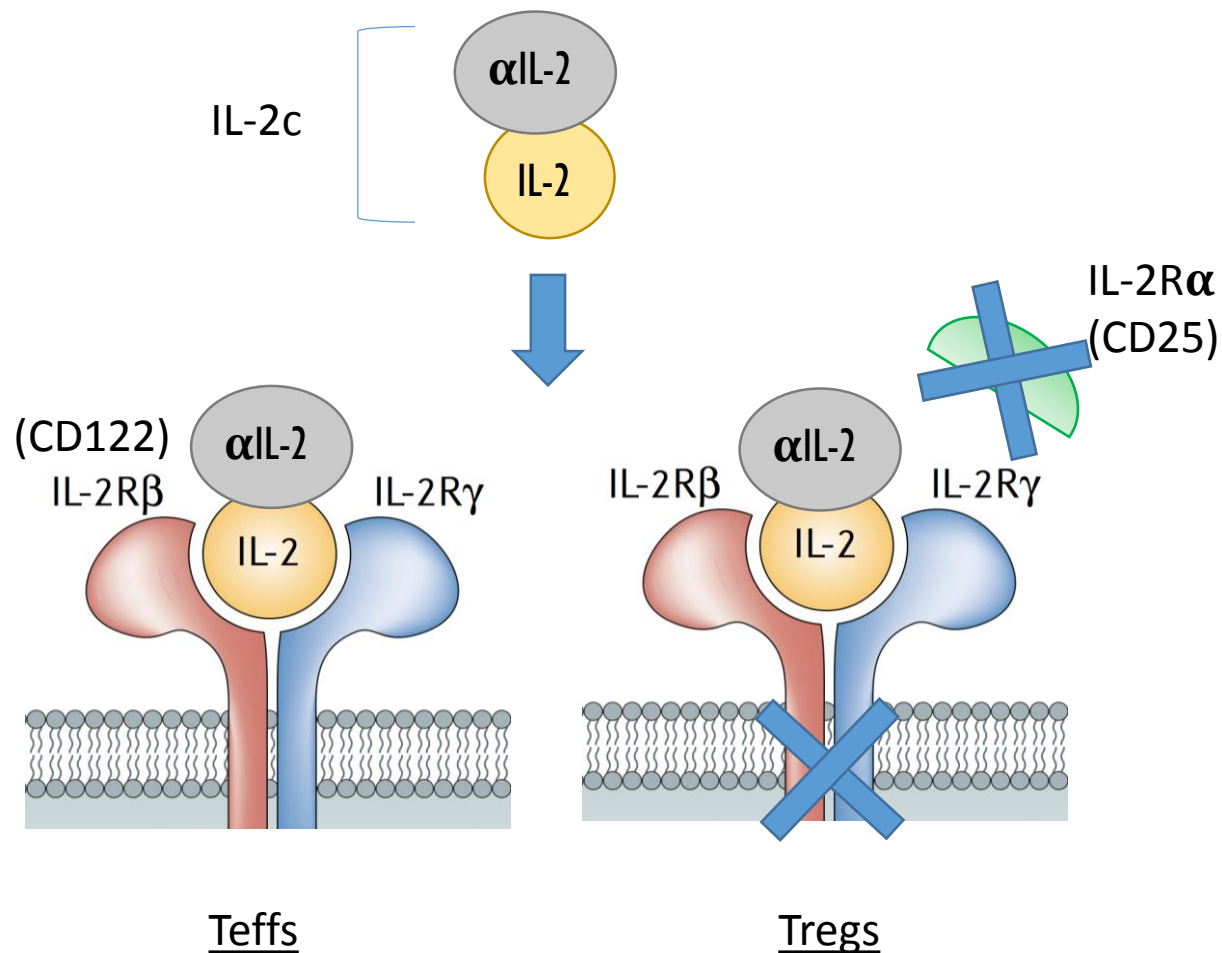
**CD4+FoxP3+ Regulatory T cells
(Tregs)**



Tumor Promoting

[Nat Rev Immunol.](#) 2018 Oct;18(10):648-659

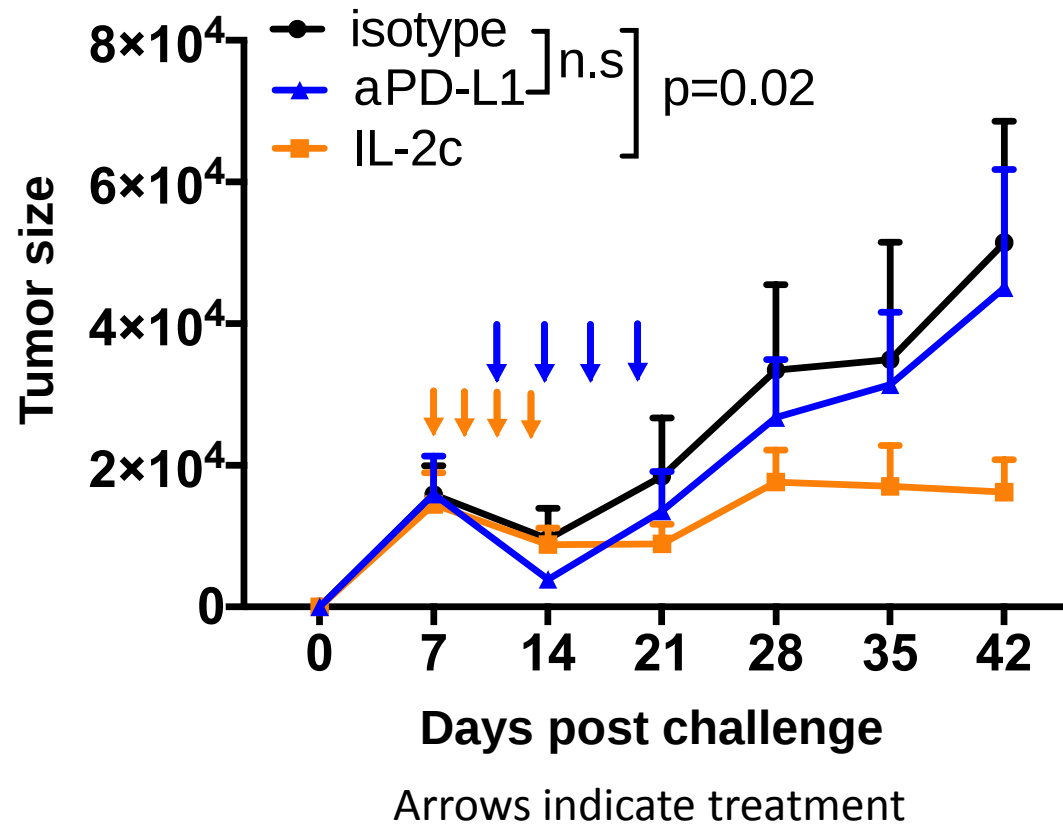
CD122-selective IL-2 complexes (IL-2c)



Immunity. 2015;42(5):815-25.

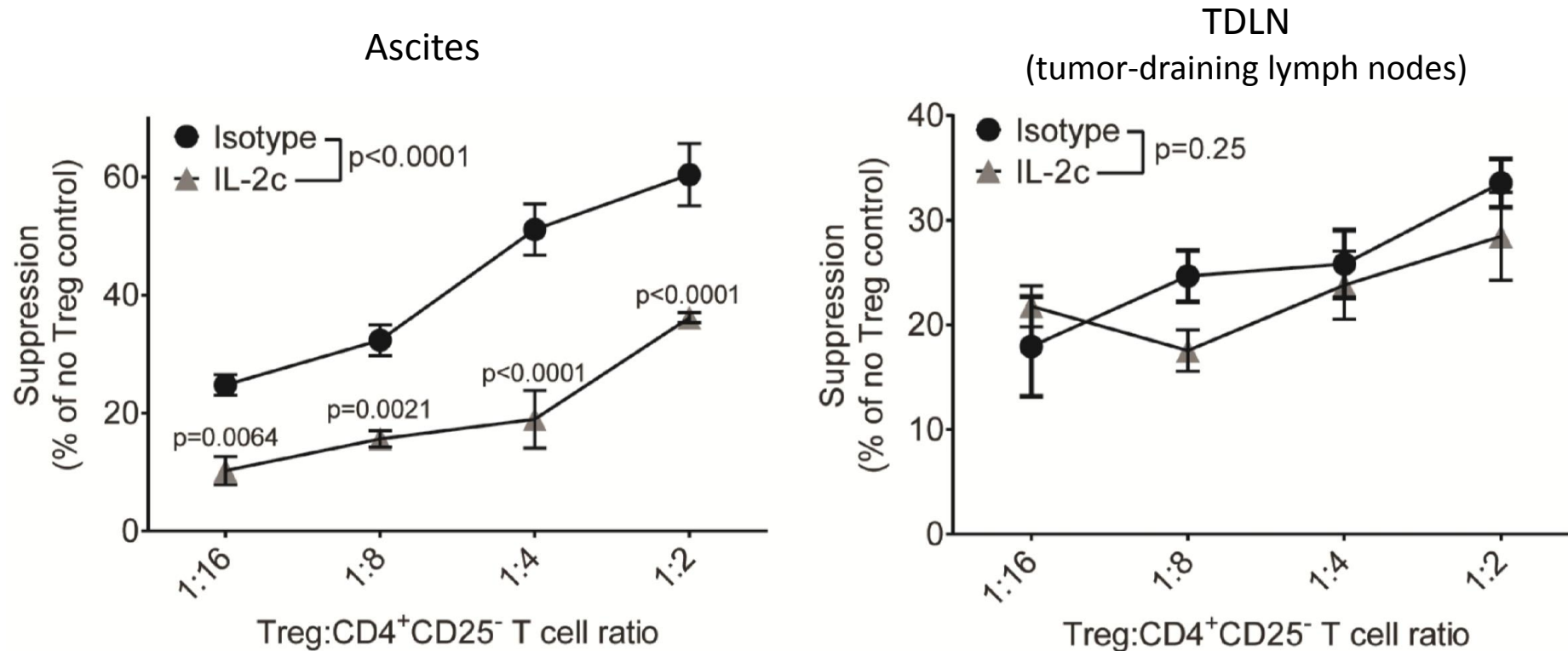
IL-2c, but not α PD-L1, significantly inhibited mouse OC growth

C57BL/6 ID8agg-Luciferase mouse ovarian cancer model



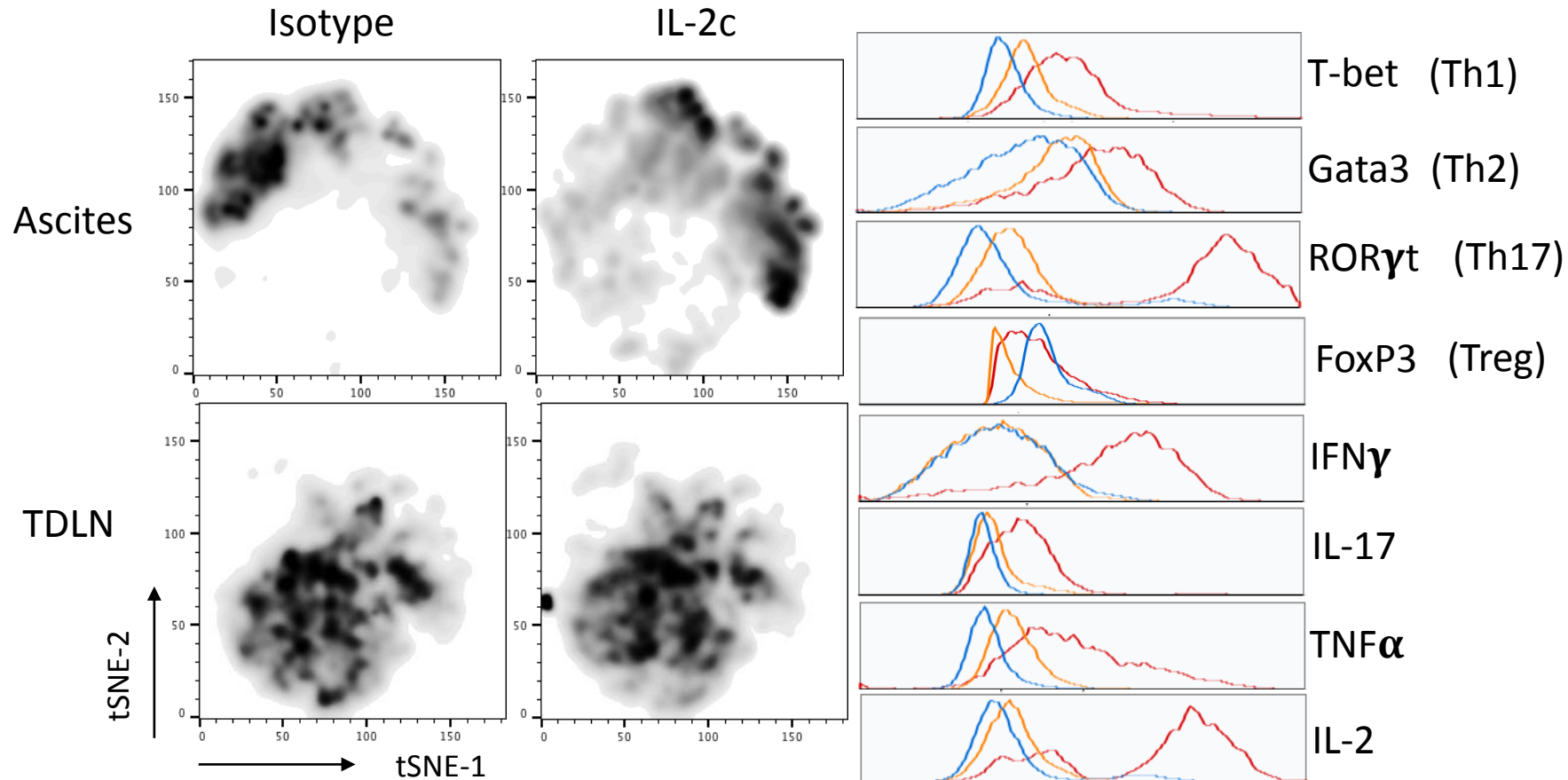
IL-2c inhibits intra-tumoral Treg suppressive function

Number of CD4⁺CD25^{hi}FoxP3⁺ cells is higher in the ascites of IL-2c treated mice.



IL-2c derails intra-tumoral Treg differentiation

tSNE analysis of CD4⁺CD25^{hi}FoxP3⁺ cells from ascites or TDLN of isotype or IL-2c treated mice

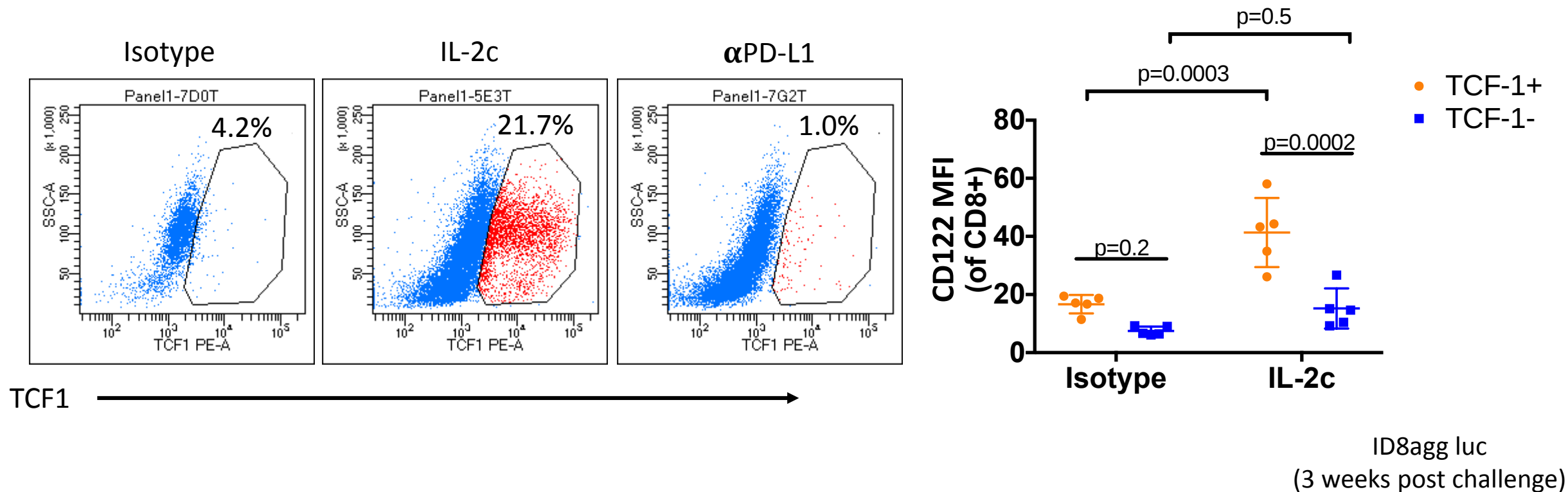


ID8agg luc
(3 weeks post challenge)

IL-2c promotes CD8⁺TCF-1⁺ T cell stem cell (TCSC)

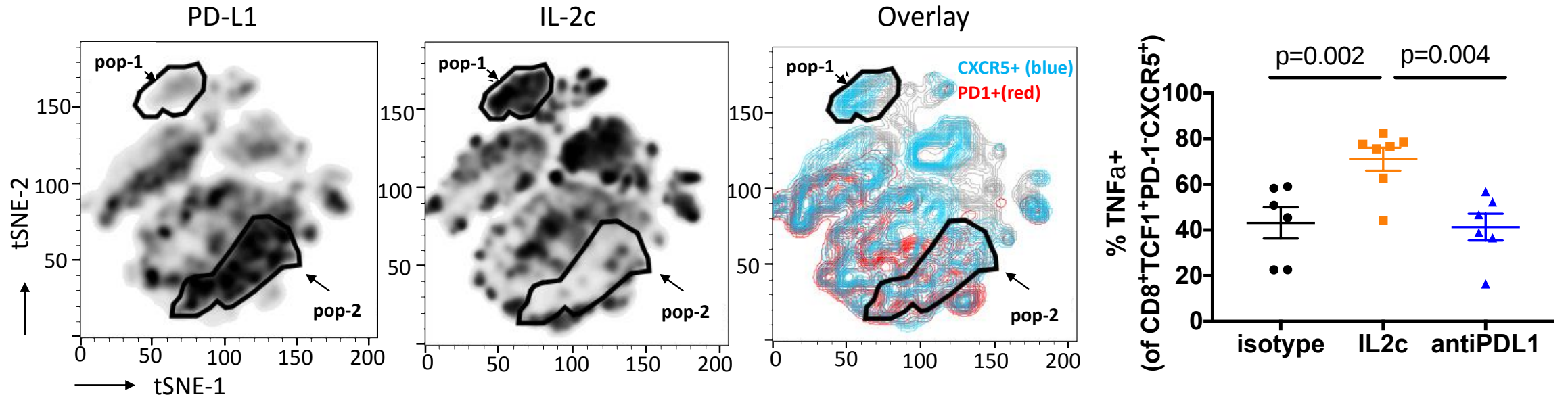
- CD8+TCF-1+ population:
 - expand in patients after α PD-L1, associated with better tumor control

CD8+ T cells in isotype, IL-2c or α PD-L1 treated tumors



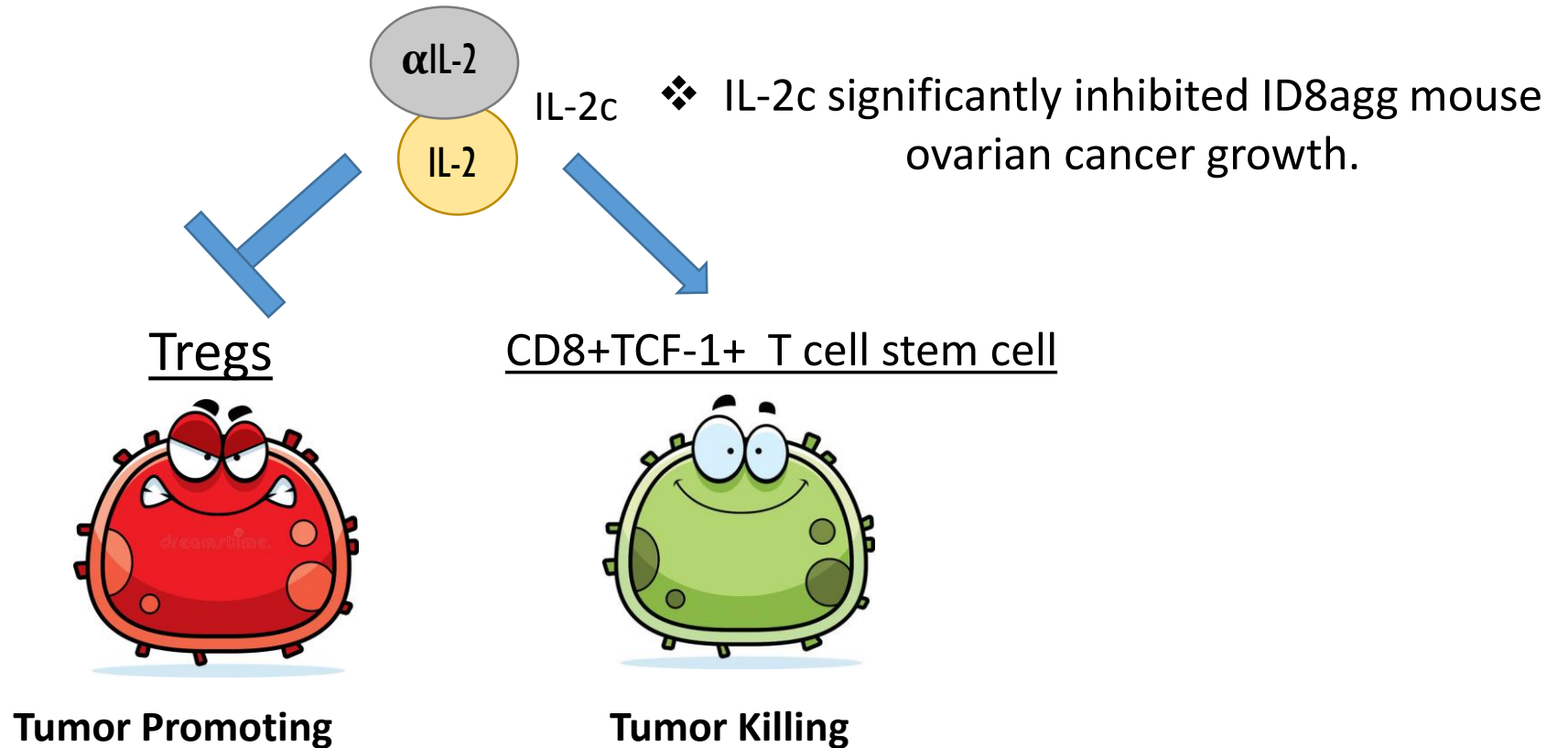
IL-2c induced distinct TCSC compared with α PD-L1

tSNE analysis of CD8⁺TCF-1⁺ immune phenotype induced by IL-2c or α PD-L1



ID8agg luc
(3 weeks post challenge)

Conclusions



- ❖ IL-2c inhibits intra-tumoral Treg suppressive function at least in part through disrupting Treg differentiation.

- ❖ IL-2c promotes CD8+TCF1+CXCR5+PD-1- T cell stem cells.

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Thank you